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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,410	05/29/2007	Deborah Hurst	PP020110.0005/59516-313	5534

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,410	HURST ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25 and 33-39* is/are pending in the application.

4a) Of the above claim(s) *16-21 and 33-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/19/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of group II, claims 1-15, a method for treating chronic lymphocytic leukemia, using an anti-CD52 antibody and a variant of IL-2 in the reply filed on 01/27/09 is acknowledged.

The traversal is on the ground(s) as follows:

As noted by the Examiner, the present application is a national phase filing of PCT~S2004/017921 filed under 35 U.S.C. 371. Accordingly, questions of unity must be resolved using the criteria of Rule 13 of the Patent Cooperation Treaty (PCT). As the Examiner has pointed out and as explained in 37 CFR 1.475(b)(2), when claims to different categories are present in the application, such as a product and a process of use of said product, the claims will be considered to have unity of invention.

Here, the claims of Group II, directed to a method of treating chronic lymphocytic leukemia using an anti-CD52 antibody and a variant of interleukin-2, and the claims of Group III, drawn to an anti-CD52 antibody and a variant of interleukin-2, should be examined together since they are directed to a product and a process of use of that product.

This is not found persuasive because of the following reasons:

Groups I-III of the claimed inventions do not relate to a single general inventive concept because they lack the same or corresponding special technical feature. According to PCT Rule 13.2, unity of invention exists only when the shared same or corresponding technical feature is a contribution over the prior art. The inventions listed as groups I-III do not relate to a single general inventive concept because they lack the same or corresponding special technical feature.

The technical feature of group I, an interleukin-2 or an anti-CD52 antibody is known in the art, as taught by Kay et al, 1988, Nouv Rev Fr Hematol, 30: 475-478, IDS of 04/19/07 or Regier et al, Feb 2004, Leukemia & Lymphoma, 45(2): 345-349, respectively. Thus the claimed invention lacks novelty and does not make a contribution over the prior art.

The requirement is still deemed proper and is therefore made FINAL.

After review and reconsideration, claims 1-15,, a method for treating chronic lymphocytic leukemia using an anti-CD52 antibody and an interleukin-2 are rejoined with group II, claims 1-15, a method for treating chronic lymphocytic leukemia, using an anti-CD52 antibody and a variant of IL-2, in view that a method for treating chronic lymphocytic leukemia using an anti-CD52 antibody and an interleukin-2 is known in the art (see Kay et al, 1988, Nouv Rev Fr Hematol, 30: 475-478, IDS of 04/17/09 and Regier et al, Feb 2004, Leukemia & Lymphoma, 45(2): 345-349).

Claims 22-25 are withdrawn as drawn to non statutory subject matter with "use" claims. As such these claims are withdrawn from consideration.

Accordingly, claims 1-15are examined in the instant application.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 is indefinite, because it is not clear what zig and p.g. are, which are not art recognizable dosage units used for the mutant interleukin Aldesleukin. In the specification, the weekly dose of aldesleukin is in the range of 1100ug to 2565 ug, which dosage provides at least 50% of the NK stimulatory activity of the total weekly dose of aldesleukin (p.7, first paragraph).

Claim Rejections - 35 USC § 112, First Paragraph, Scope

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for a method for treating chronic lymphocytic leukemia, using an anti-CD52 antibody and an interleukin-2 or a variant thereof, does not reasonably provide enablement for a method for treating chronic lymphocytic leukemia, using **a fragment** of an anti-CD52 antibody, Alemtuzumab, and an interleukin-2 or a variant thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

To comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, the specification must enable one skilled in the art to make and use the claimed invention without undue experimentation. The claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows: (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

One would not know how to use the claimed method, because an immunologically active fragment of an anti-CD52 antibody does not necessarily bind to the CD52 antigen, in view that any peptide fragment would be immunologically active, i.e., producing an immune response.

MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In constrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Given the above, and in view of the complex nature of the invention, a lack of sufficient disclosure in the specification, and little is known in the art concerning the claimed invention, there would be an undue quantity of experimentation required for one of skill in the art to practice the claimed invention, that is commensurate in scope of the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 1-2, 4-9, 11-13, are rejected under 35 U.S.C. 103(a) as being unpatentable over Regier et al, Feb 2004, Leukemia & Lymphoma, 45(2): 345-349), in view of Kay et al, 1988, Nouv Rev Fr Hematol, 30: 475-478, IDS of 04/17/09, and further in view of Denis-Mize et al, 2003, J Immunother, 26 (6), S43, abstract only, and Dmoszynska et al, 1999, Leukemia & Lymphoma, 34(3-4): 335-340, IDS of 04/17/09.

Claims 1-2, 4-9, 11-13, are as follows:

1. (Original) A method of treating chronic lymphocytic leukemia in a human subject, said method comprising administering to said subject at least one cycle of concurrent therapy with an anti-CD52 antibody and an interleukin-2 (IL-2).

2. (Original) The method of claim 1, wherein said IL-2 is recombinantly produced IL-2 having an amino acid sequence for human IL-2 or a variant thereof having at least 70% sequence identity to the amino acid sequence for human IL-2.

4. (Currently Amended) The method of claim 1, wherein said anti-CD52 antibody is an immunologically active anti-CD52 antibody.

5. (Original) The method of claim 4, wherein said anti-CD52 antibody is Alemtuzumab or fragment thereof.

6. (Original) A method of treating chronic lymphocytic leukemia in a human subject, said method comprising administering to said subject at least one cycle of concurrent therapy with an anti-CD52 antibody and an interleukin-2 (IL-2), wherein said cycle comprises administering a therapeutically effective dose of an anti- CD52 antibody according to a weekly,

twice-weekly, or thrice-weekly dosing schedule in combination with administration of a constant IL-2 dosing regimen, said constant IL-2 dosing regimen comprising administering a total weekly dose of an IL-2 to said subject.

7. (Original) The method of claim 6, wherein a first dose of an IL-2 is administered to said subject concurrently with a first dose of an anti-CD52 antibody.

8. (Original) The method of claim 7, wherein a first dose of an IL-2 is administered to said subject one week after a first dose of an anti-CD52 antibody is administered to said subject.

9. (Currently Amended) The method of claim 6, wherein said IL-2 is recombinantly produced IL-2 having an amino acid sequence for human IL-2 or a variant thereof having at least 70% sequence identity to the amino acid sequence for human IL-2.

11. (Original) The method of claim 6, wherein said anti-CD52 antibody is an immunologically active anti-CD52 antibody.

12. (Original) The method of claim 11, wherein said anti-CD52 antibody is Alemtuzumab or fragment thereof.

13. (Original) The method of claim 6, wherein one or more subsequent cycles of concurrent therapy with IL-2 and anti-CD52 antibody is initiated about 1 month to about 6 months following completion of a first cycle or completion of any subsequent cycles of concurrent therapy with IL-2 and anti-CD52 antibody.

Rieger et al teach treating chronic lymphocytic leukemia (CLL) using Alemtuzumab, which is a humanized anti-CD52 antibody (abstract, and p.345). Rieger et al suggests flexible time intervals for the anti-CD52 antibody injection, depending on leukocytes counts, because

application three times a week at a dose of 30mg each for 12 weeks causes hematotoxicity in many patients (abstract, p.347).

Regier et al do not teach: 1) a combination of anti-CD52 antibody and interleukin-2 (IL-2) for treating CLL, 2) administration of CD52 antibody weekly or twice-weekly, and a total weekly dose of IL-2, 3) administration of anti-CD52 antibody and IL-2 by separate, sequential or simultaneous administration, or administration of a first dose of an IL-2 concurrent with or one week after a first dose of an anti-CD52 antibody and 4) initiation of one or more subsequent cycles of concurrent therapy with IL-2 and anti-CD52 antibody at about 1 month to about 6 months following completion of a first cycle or completion of any subsequent cycles of concurrent therapy with IL-2 and anti-CD52 antibody.

Kay et al teach using recombinant IL-2 for treating CLL because CLL is associated with deficiency in IL-2 (abstract, p.477, item under Discussion), and that IL-2 reduces growth of CLL (abstract).

Denis-Mize et al teach that a combination with IL-2 would improve the efficacy and durability of anti-cancer monoclonal antibody therapy (abstract, first two lines). Denis-Mize et al teach that interleukin-2 (Aldesleukin), which is used in phase I clinical trail of Non-Hodgkin's lymphoma, acts by increasing T cells and NK activity, such as NK-mediated antibody dependent cellular cytotoxicity (ADCC) and cytolytic killing, which is measured by standard 51Cr release assay (abstract).

Dmoszynska et al teach that administration of IL-2 in CLL induces a marked increase in T cell subsets and NK cells (abstract, p.337 and Tables II-III on p.337).

It would have been prima facia obvious to one of ordinary skill in the art at the time the invention was made to combine anti-CD52 antibody taught by Regier et al with interleukin-2 taught by Kay et al for treating CLL, because: 1) CLL is associated with deficiency in the therapeutic IL-2 as taught by Kay et al, 2) A combination with IL-2 would improve the efficacy and durability of anti-cancer monoclonal antibody therapy, as suggested by Denis-Mize et al, because IL-2 acts by increasiing in the activity of T cells and NK activity, such as NK-mediated antibody dependent cellular cytotoxicity and cytolytic killing. Such increase in the activity of T cells and NK cells activity by IL-2 also occurs in CLL patients treated with IL-2, as taught by Dmoszynska et al, and 3) The two methods act by different ways and thus would complement each other, i.e, cancer cell killing via anti-CD52 antibody action versus increasing the immune response via increasing the activity of T cells and NK cells, which NK cells would mediate and thus enhancing the ADCC activity of the antibody used in the immunotherapy, in view of the teaching of Denis-Mize et al. One would have been motivated to do so to enhance the efficacy of CLL treatment.

Concerning the frequency and how anti–CD52 antibody and IL-2 are administered relative to each other, determination of optimum conditions is within the level of one of ordinary skill in the art. To determine optimum concentration of reactants is within the level of ordinary skill in the art. See *In re Kronig*, 190 USPQ 425, and because "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See also *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

2. Claims 2-3, 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Regier et al, Feb 2004, Leukemia & Lymphoma, 45(2): 345-349), in view of Kay et al, 1988, Nouv Rev Fr Hematol, 30: 475-478, IDS of 04/17/09, Denis-Mize et al, 2003, J Immunother, 26 (6), S43, abstract only, and Dmoszynska et al, 1999, Leukemia & Lymphoma, 34(3-4): 335-340, IDS of 04/17/09, as applied to claims 1-2, 4-9, 11-13 above, and further in view of Mark et al (US 4,518,584, filed on 12/20/1983).

Claims 2-3, 9-10 are as follows:

2. (Original) The method of claim 1, wherein said IL-2 is recombinantly produced IL-2 having an amino acid sequence for human IL-2 or a variant thereof having at least 70% sequence identity to the amino acid sequence for human IL-2.

3. (Original) The method of claim 2, wherein said variant thereof is des-alanyl-1, serine 125 human interleukin-2.

9. (Currently Amended) The method of claim 6, wherein said IL-2 is recombinantly produced IL-2 having an amino acid sequence for human IL-2 or a variant thereof having at least 70% sequence identity to the amino acid sequence for human IL-2.

10. (Original) The method of claim 9, wherein said variant thereof is des-alanyl-I, serine 125 human interleukin-2.

The teaching of Regier et al, Kay et al, Denis-Mize et al, and Dmoszynska et al has been set forth above.

Regier et al, Kay et al, Denis-Mize et al, and Dmoszynska et al do not teach the use of anti-CD52 antibody with IL-2 variant or des-alanyl-1, serine 125 human interleukin-2 in treating CLL.

Mark et al teach making an IL-2 variant, des-alanyl-1, serine 125 human interleukin-2, where alanyl-1 is deleted and cysteine 125 is replaced with serine to eliminate intermolecular crosslinking or incorrect intramolecular disulfide bond formation (claim 4, and column 3, paragraph under "Modes for carrying out the invention""). Mark et al teach that des-alanyl-1, serine 125 human interleukin-2 (pLW46) has a higher IL-2 activity that of the native IL-2 control (column 18, Table II and paragraph under Table II).

It would have been prima facia obvious to one of ordinary skill in the art at the time the invention was made to replace the native IL-2 in the combination of anti-CD52 antibody and IL-2 taught by Regier et al, Kay et al, Denis-Mize et al, and Dmoszynska et al, with an IL-2 variant, des-alanyl-1, serine 125 human interleukin-2, taught by Mark et al, for enhancing the efficacy of treatment CLL, because des-alanyl-1, serine 125 human interleukin-2 is more advantageous than native IL-2, i.e., having higher IL-2 activity than native IL-2, in view of the teaching of Mark et al.

3. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Regier et al, Feb 2004, Leukemia & Lymphoma, 45(2): 345-349), in view of Kay et al, 1988, Nouv Rev Fr Hematol, 30: 475-478, IDS of 04/17/09, Denis-Mize et al, 2003, J Immunother, 26 (6), S43, abstract only, as applied to claims 1-2, 4-9, 11-13 above, and Dmoszynska et al, 1999, Leukemia & Lymphoma, 34(3-4): 335-340, IDS of 04/17/09, and further in view of Ayanlar-Baturnan et al, 1986, Blood, 67(2): 279-284.

Claim 14. (Original) The method of claim 13, wherein T-cell counts are monitored in said subject to determine when each of said cycles is initiated, said cycles being initiated when T-cell

count is less than 80% of the T-cell count at the conclusion of any previous cycle of concurrent therapy with an IL-2 and an anti-CD52 antibody.

The teaching of Regier et al, Kay et al, Denis-Mize et al, and Dmoszynska et al has been set forth above.

Regier et al, Kay et al, Denis-Mize et al, and Dmoszynska et al do not teach monitoring T cell count to determine when each cycles of anti-CD52 antibody and IL-2 treatment is initiated, said cycles being initiated when T-cell count is less than 80% of the T-cell count at the conclusion of any previous cycle of concurrent therapy with an IL-2 and an anti-CD52 antibody.

Ayanlar-Baturnan et al teach that T lymphocytes of CLL patients are defective in IL-2 production (p.279, first column, third paragraph). Ayanlar-Baturnan et al teach that the response in CLL patients to IL-2 is measured by the increase in the T cell proliferation (abstract, first column).

It would have been prima facia obvious to one of ordinary skill in the art at the time the invention was made to treat CLL, using the combination of anti-CD52 antibody and IL-2 taught by Regier et al, Kay et al, Denis-Mize et al, and Dmoszynska et al, supra. It would have been obvious to monitor T cell count to determine when each cycles of anti-CD52 antibody and IL-2 treatment is initiated after the first cycle of treatment with anti-CD52 antibody and IL-2, because: 1) the response to IL-2 in CLL patients is measured by the increase in the T cell proliferation, as taught by Ayanlar-Baturnan et al, and 2) rIL-2 significantly increases the amount of T cells in treated CLL patients as taught by Dmoszynska et al.

Concerning initiation of anti-CD52 antibody and IL-2 treatment when T-cell count is less than 80% of the T-cell count at the conclusion of any previous cycle of concurrent therapy with

an IL-2 and an anti-CD52 antibody, determination of optimum conditions is within the level of one of ordinary skill in the art. To determine optimum concentration of reactants is within the level of ordinary skill in the art. See *In re Kronig*, 190 USPQ 425, and because "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See also *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

4. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Regier et al, Feb 2004, Leukemia & Lymphoma, 45(2): 345-349), in view of Kay et al, 1988, Nouv Rev Fr Hematol, 30: 475-478, IDS of 04/17/09, Denis-Mize et al, 2003, J Immunother, 26 (6), S43, abstract only, and Dmoszynska et al, 1999, Leukemia & Lymphoma, 34(3-4): 335-340, IDS of 04/17/09, as applied to claims 1-2, 4-9, 11-13 above, and further in view of Safar et al, 2000, Immunopharmacol, 49: 419-423.

Claim 15. (Original) The method of claim 6, wherein said total weekly dose of an IL-2 is in an amount that provides at least 50% of the NK stimulatory activity of a total weekly dose of Aldesleukin administered in a range of from about 1100 zig to about 1834 p. g.

The teaching of Regier et al, Kay et al, Denis-Mize et al, and Dmoszynska et al has been set forth above.

Regier et al, Kay et al, Denis-Mize et al, and Dmoszynska et al do not teach total weekly dose of an IL-2 is in an amount that provides at least 50% of the NK stimulatory activity of a

total weekly dose of Aldesleukin administered in a range of from about 1100 zig to about 1834 p. g.

Safar et al teach that Aldesleukin has been recommended by FDA for clinical treating cancer patients, such as metastatic renal and melanoma, and is also increasingly being widely used in innovative immunotherapic applications (abstract, p.419-420).

It would have been prima facia obvious to one of ordinary skill in the art at the time the invention was made to treat CLL, using the combination of anti-CD52 antibody and IL-2 taught by Regier et al, Kay et al, Denis-Mize et al, and Dmoszynska et al, supra. It would have been obvious to use IL-2 in a concentration that stimulates NK activity, similar to that used for the mutant interleukin-2 Aldesleukin, such as in an amount that provides at least 50% of the NK stimulatory activity of a total weekly dose of Aldesleukin as a reference, because Aldesleukin has been recommended by FDA for clinical treating cancer patients, such as metastatic renal and melanoma, and is also increasingly being widely used in innovative immunotherapic applications, as taught by Safar et al, such as in Phase I clinical treatment of Non-Hodgkin's lymphoma, taught by Denis-Mize et al.

Moreover, determination of optimum conditions is within the level of one of ordinary skill in the art. To determine optimum concentration of reactants is within the level of ordinary skill in the art. See *In re Kronig*, 190 USPQ 425, and because "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See also *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
March 20, 2008

/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643